# ADVISORY – ACUTE HEPATITIS OF UNKNOWN ETIOLOGY AND POTENTIAL LINK TO ADENOVIRUS INFECTION AMONG CHILDREN

**Date: May 6, 2022**

**Key Messages:**

- Between October 2021 and April 25, 2022, 169 cases of acute severe hepatitis in children aged one month to 16 years have been reported across 12 countries.
- The severity of the disease in these young, otherwise healthy children is concerning and the cause is under active investigation globally.
- Seventeen children (approximately 10%) have required a liver transplant. To date one child has been reported to have died of liver failure.
- These global cases tested negative for the usual viral causes of hepatitis A, B, C, D, and E, as well as other viruses that can occasionally cause hepatitis (e.g., Epstein Barr Virus and Cytomegalovirus).
- A detailed report from the UK indicated that Adenovirus was detected in 74 of 85 cases tested; 18 were identified as type 41
- SARS-CoV-2 was detected in less than 10 % of cases tested so far
- Given the complexity of diagnosis, when a case of acute hepatitis is identified in children (age less than 16 years), clinicians are strongly advised to consult with pediatric hepatology, infectious diseases, and microbiology.
- Any cases that do not have a clear etiology of severe hepatitis in children 16 years of age or younger are reportable to public health. Pediatric hepatology at BC Children's Hospital can assist with determination of reportability.
- Further updates, including case definition and reporting processes, will be available at http://www.bccdc.ca/health-professionals/clinical-resources/acute-hepatitis-children

**Ministry of Health**

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**Background:**

- As of April 20, 2022, at least 169 cases of acute hepatitis of unknown etiology have been reported in pediatric patients (1 month to 16 years old) from 11 countries in the WHO European Region and one country in the WHO Region of the Americas.[1]
- According to the European Centre for Disease Prevention and Control (ECDC), UK laboratory investigations excluded viral hepatitis types A, B, C, D and E in all cases.
- Detailed information collected about food, drink and personal habits has not identified any common exposure, including COVID-19 vaccines.[2]
- The UK Health Security Agency (UKHSA) has identified adenovirus as the most common pathogen in 40 of 53 (75%) confirmed cases of sudden onset of acute hepatitis (liver inflammation) in children under the age of 10 years.[3]
- While adenovirus is a possible hypothesis, investigations are ongoing to identify the causative agent.[4] The BC Centre for Disease Control (BCCDC), BC Children's Hospital and BC Women's Hospital are aware and monitoring this emerging issue.

**Recommendations for Infection Prevention and Control**

- Diligent adherence to contact/droplet precautions for hepatitis of possible infectious etiology is recommended. Additionally, health care workers should perform a point of risk assessment (PCRA) to determine any specific or additional IPC measures.
- Patients should be managed by following local health authority IPC or the Public Health Agency of Canada's Routine Practices and Additional Precautions for Preventing the Transmission of Infection in Healthcare Settings guidance.

**Recommendations for Patient Management**

- Severe acute hepatitis carries a high mortality in the pediatric population. Early consultation with pediatric hepatology, infectious diseases, and microbiology is strongly recommended to ensure timely care and investigations. **Consultation is available through the BC Children's Hospital switchboard at 604 875 2345.**

- Monitoring for Symptoms
    - *Hepatitis (A to E):* Symptoms include fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine, light-colored stools, joint pain and/or jaundice.[5] Cases of sudden onset hepatitis in the UK have predominately been in children under 5 years old with initial symptoms of gastroenteritis illness (diarrhea and nausea) followed by jaundice.[6] Treatment of hepatitis depends on underlying etiology.[7]

1 World Health Organization (WHO). (2022, April 23). Multi-country – acute, severe hepatitis of unknown origin in children.
2 The European Centre for Disease Prevention and Control (ECDC). (2022, April 19). Update: Hepatitis of unknown origin in children.
3 UK Health Security Agency (UKHSA). (2022, April 6). Increase in hepatitis (liver inflammation) cases in children under investigation.
4 World Health Organization (WHO). (2022, April 23). Multi-country – acute, severe hepatitis of unknown origin in children.
5 BC Centre for Disease Control (BCCDC). (2022). Hepatitis.
6 UK Health Security Agency (UKHSA). (2022, April 6). Increase in hepatitis (liver inflammation) cases in children under investigation.
7 The Centers for Disease Control and Prevention (CDC). (2022, April 21). Recommendations for adenovirus testing and reporting of children with acute hepatitis of unknown etiology.

- *Adenovirus:* Symptoms include common cold or flu-like symptoms, fever, sore throat, cough, conjunctivitis, abdominal pain, diarrhea and vomiting.[8] There is no specific treatment for adenovirus infections.[9]

- Testing & Investigations
  - Testing for following pathogens/aetiologies is advised in consultation with pediatric infectious diseases and microbiology:
    - Hepatitis A, B, C, and E; Hepatitis D should be considered for patients positive for Hep B
    - Cytomegalovirus and Epstein-Barr virus
    - SARS-CoV-2 (PCR and serology), influenza, RSV
    - Adenovirus: A Nucleic Acid Amplification Test (NAAT) (e.g., PCR) is preferable and may be done on respiratory specimens, stool or rectal swabs, or blood.[10]
      - Indicate "Undiagnosed Acute Hepatitis" under the "Reason for Test" section of the lab requisition.
      - Respiratory and stool samples can be sent to most local laboratories for adenovirus testing.
      - Blood and other samples should be sent to the BC Children's and Women's Hospital Microbiology Laboratory.
      - Samples positive for adenovirus are forwarded to the BCCDC Public Health Laboratory for strain typing.
    - Wilson's Disease: ceruloplasmin
    - Autoimmune: ANA, Ig

  - The differential for undifferentiated hepatitis is broad, and investigations should be guided by the clinical picture in consultation with pediatric sub-specialty services. Other causes of hepatitis, including non-infectious causes, should be considered:
    - Infectious: (Parvovirus B19, HSV, HHV-6, VZV, HIV, Enterovirus, Norovirus, Rotavirus, Leptospirosis, Tuberculosis, Lymphocytic choriomeningitis virus etc.)
    - Toxic: acetaminophen, prescription medications, mushroom poisoning etc.
    - Vascular: shock and portal hypertension
    - Inborne errors of metabolism
    - Heat stroke
    - Malignancy
    - Muscle disorders (i.e. polymyositis )

8 The Centres for Disease Control and Prevention (CDC). (2019, August 28). Adenovirus.

9 The Centers for Disease Control and Prevention (CDC). (2022, April 21). Recommendations for adenovirus testing and reporting of children with acute hepatitis of unknown etiology.

10 The Centers for Disease Control and Prevention (CDC). (2022, April 21). Recommendations for adenovirus testing and reporting of children with acute hepatitis of unknown etiology.

**Reporting**

- Given the possible infectious etiology of this disease the Provincial Health Officer (PHO) has determined that, per the case definition, the following are reportable communicable diseases under the Reporting Information Affecting Public Health Regulation of the *Public Health Act*.

    - Cases of severe hepatitis (AST/ALT >500 IU/L) of unknown origin in children aged 16 and younger. Pediatric hepatologists at BCCH can assist with determination of reportability.

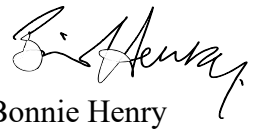
    - A person presenting with an acute hepatitis (non hep A-E) of any age who is a close contact of a case since 1 October 2021.

- Clinicians must report to their regional public health office any child 16 years of age or younger with hepatitis of unknown etiology and elevated AST and ALT (>500 IU/L). Contact information for regional public health is available in Appendix 1:

**Additional Resources:**

- BCCDC Acute Hepatitis Children: http://www.bccdc.ca/health-professionals/clinical-resources/acute-hepatitis-children
- The BCCDC Public Health Laboratory: www.bccdc.ca/our-services/service-areas/bccdc-public-health-laboratory
- US CDC information on Adenovirus: www.cdc.gov/adenovirus/index.html
- UK Technical Briefing: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1073704/acute-hepatitis-technical-briefing-2.pdf
- Reporting Information Affecting Public Health Regulation: https://www.bclaws.gov.bc.ca/civix/document/id/complete/statreg/167_2018#division_d1e787

Sincerely,



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**Appendix 1: Regional Public Health contact information (for health professionals only)**

- Fraser Health: 1-866-990-9941
- Interior Health: 1-866-457-5648
- Island Health
    - South Island: 1-866-665-6626
    - Central Island: 1-866-770-7798
    - North Island: 1-877-887-8835
- Northern Health:
    - Business hours: 250-645-3794
    - After business hours: 250-565-2000, press 7, ask for the MHO on call
- Vancouver Coastal Health:
    - Business hours: 1-855-675-3900
    - After business hours: 604-527-4893